(FILE 'HOME' ENTERED AT 14:59:49 ON 19 FEB 2008)

FILE 'REGISTRY' ENTERED AT 15:02:00 ON 19 FEB 2008
L1 STRUCTURE UPLOADED
L2 12 S L1 SSS FULL

FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE' ENTERED AT 15:07:47 ON 19 FEB 2008
L3 86 S L2 OR 4 HYDROXY L ISOLEUCINE
L4 2 S L3 AND (INSULIN RESISTANCE OR INSULIN SENSITIZING OR INSULIN
L5 2 DUP REM L4 (0 DUPLICATES REMOVED)
L6 17 S L3 AND (COMBINATION OR COMB? OR CONCURRENT? OR COADMINISTRA?
L7 17 FOCUS L6 1-

=> s l3 and (diabetes or diabetic)
L8 21 L3 AND (DIABETES OR DIABETIC)

=> focus
PROCESSING COMPLETED FOR L8
L9 21 FOCUS L8 1-

=> d ibib abs 1-21

L9 ANSWER 1 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1173498 CAPLUS
DOCUMENT NUMBER: 145:471854
TITLE: Preparation of diastereoisomers of 4-hydroxyisoleucine
INVENTOR(S): Coquelet, Claude; Mioskowski, Charles; Wagner, Alain
PATENT ASSIGNEE(S): Innodia Inc., Can.; Conseil National de la Recherche Scientifique (C.N.R.S.); Universite Louis Pasteur Strasbourg I
SOURCE: PCT Int. Appl., 42pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006117696	A2	20061109	WO 2006-IB1758	20060217
WO 2006117696	A3	20070125		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

AU 2006242851 A1 20061109 AU 2006-242851 20060217

CA 2598491 A1 20061109 CA 2006-2598491 20060217

EP 1853552 A2 20071114 EP 2006-765601 20060217

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR

IN 2007DN06046 A 20070817 IN 2007-DN6046 20070802

PRIORITY APPLN. INFO.: US 2005-654413P P 20050218

WO 2006-IB1758 W 20060217

AB The invention relates to configurational isomers of 4-hydroxyisoleucine, intermediate lactones, and pharmaceutically-acceptable salts and prodrugs. The isomers of the invention exhibit insulinotropic activity and thus may be useful for the prevention and treatment of disorders of carbohydrate or lipid metab., including ***diabetes*** mellitus (type 1 and type 2 ***diabetes***), pre- ***diabetes*** , and metabolic syndrome. Thus, treatment of imine EtO2CCH:NHC6H4OMe-p with 2-butanone in the presence of L-proline afforded adduct (2S,3S)-EtO2CCH(NHC6H4OMe-p)CHMeCOMe. Epimerization at C-3 was achieved with DBN to yield the 2S,3R isomer. Deprotection with ammonium nitrate and redn. with KBH4 and concomitant cyclization afforded the lactone, which underwent hydrolysis with LiOH to afford (2S,3R,4S)-4-hydroxyisoleucine. The configurational isomers of 4-hydroxyisoleucine were examd. for stimulation of glucose uptake by differentiated 3T3-L1 adipocyte cells and for glucose-dependent stimulation of insulin secretion in INS-1 cells.

L9 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:919628 CAPLUS

DOCUMENT NUMBER: 145:315262

TITLE: Preparation of 4-hydroxyisoleucine analogs for treatment of ***diabetes***

INVENTOR(S): Mioskowski, Charles; Marin, Sandra De Lamo; Maruani, Martine; Gill, Manjinder

PATENT ASSIGNEE(S): Fr.

SOURCE: U.S. Pat. Appl. Publ., 80pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006199853	A1	20060907	US 2006-356848	20060217
AU 2006245438	A1	20061116	AU 2006-245438	20060217
CA 2598365	A1	20061116	CA 2006-2598365	20060217
WO 2006120574	A2	20061116	WO 2006-IB1666	20060217
WO 2006120574	A3	20070510		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

EP 1858840	A2	20071128	EP 2006-765562	20060217

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU

IN 2007DN06514	A	20070907	IN 2007-DN6514	20070822

PRIORITY APPLN. INFO.: US 2005-654342P P 20050218
WO 2006-IB1666 W 20060217
OTHER SOURCE(S): MARPAT 145:315262

AB The invention relates 4-hydroxyisoleucine analogs R4-X-CR1aR1bCR2aR2bCR3(B)A [A is a (thio)carboxylic acid, ester or amide, an acyl group, SO3H, etc.; B is an amino group, including N-protected amino; X is O, S, NH or substituted imino; R1a, R1b, R2a, R2b, R3, R4 are H, (un)substituted alkyl, cycloalkyl, etc.; R1a and R2a may combine to form a ring; R2a and R2b may be CO, alkylimino, or alkylidene] and to pharmaceutically-acceptable lactones, salts, or prodrugs, which stimulate both glucose uptake and insulin secretion and may thus be useful for the prevention and treatment of disorders of carbohydrate or lipid metab.,

including ***diabetes*** mellitus (type 1 and type 2 ***diabetes***), pre- ***diabetes*** , and metabolic syndrome. The desired products are formed via corresponding lactones, which are cleaved under basic conditions. The method is applied to the synthesis of (S,S,S)-amino(2-hydroxycyclohexyl)acetic acid, which stimulates glucose uptake by differentiated 3T3-L1 adipocytes and glucose-dependent insulin secretion in INS-1 cells.

L9 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:1019888 CAPLUS
DOCUMENT NUMBER: 142:11514
TITLE: A synergistic composition for the treatment of ***diabetes*** mellitus
INVENTOR(S): Bhaskaran, Sunil; Mohan, Vishwaraman
PATENT ASSIGNEE(S): Indus Biotech Pvt. Ltd., India
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004100968	A2	20041125	WO 2004-IB1550	20040513
WO 2004100968	A3	20050120		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1638586	A2	20060329	EP 2004-732676	20040513

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK

JP 2006528235	T	20061214	JP 2006-530649	20040513
IN 2005MN01267	A	20070629	IN 2005-MN1267	20051114
IN 2006MN00154	A	20061027	IN 2006-MN154	20060208

PRIORITY APPLN. INFO.: US 2003-470742P P 20030514
WO 2004-IB1550 W 20040513

AB The present invention relates to a synergistic compn. for the treatment of ***diabetes*** in a subject in need thereof, comprising trigonelline at concn. of 20 to 30%, amino acids at concn. of 20 to 60%, and sol. fiber at concn. of 10 to 60%, optionally along with pharmaceutically acceptable additives, a process thereof and also, a method of treating ***diabetes*** . For example, capsules of a fenugreek seed ext. contg. 20 to 60% amino acids, 20 to 30% of trigonelline, and 10 to 60% galactomannan fiber showed antidiabetic activity in lab. animals and in patients with Type II ***diabetes*** mellitus, acting at the pancreas through potassium channel-mediated insulin secretion.

L9 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1088481 CAPLUS
DOCUMENT NUMBER: 147:407090
TITLE: Preparation of 4-hydroxyisoleucine analogs and their compositions for use in the prevention and treatment of disorders of fat metabolism and obesity
INVENTOR(S): Jette, Lucie; McNicol, Patricia; Gill, Manjinder; Marette, Andre
PATENT ASSIGNEE(S): Innodia Inc., Can.
SOURCE: PCT Int. Appl., 274pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007107008	A1	20070927	WO 2007-CA471	20070322

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,

BY, KG, KZ, MD, RU, TJ, TM
US 2006223884 A1 20061005 US 2006-387534 20060322
PRIORITY APPLN. INFO.: US 2006-387534 A 20060322
US 2006-785174 A 20060322
US 2006-836648P P 20060810
US 2005-664038P P 20050322
OTHER SOURCE(S): MARPAT 147:407090
GI

AB The invention relates to 4-hydroxyisoleucine isomers, [e.g., (+)-(2S,3R,4S)-4-hydroxyisoleucine, (I)], and analogs and to their pharmaceutically acceptable lactones, salts, metabolites, solvates and/or prodrugs, to processes for their prepn., and to their pharmaceutical compns. useful for preventing and treating disorders of fat metab. and related syndromes. The invention also relates to the use of these compds. in the prevention and treatment of obesity and related syndromes including, but not limited to, the cosmetic treatment of a mammal to effect a cosmetically beneficial loss of body wt., and more particularly loss of body fat. Twenty biol. examples are given. Thus, ring opening of .gamma.-lactone II [90:10 mixt. of (2S,3R,4S) to (2S,3R,4R); prepn. given] in water in the presence of LiOH/AcOH gave I after purifn. I reduced the body wt. gain and visceral fat in diet induced obesity mice, and the triglycerides and cholesterol levels in Sprague-Dawley rats. I in combination with rosiglitazone (III) controlled the unwanted side effect of wt. gain caused by the antidiabetic agent III.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1041307 CAPLUS
DOCUMENT NUMBER: 145:397785
TITLE: Preparation of 4-hydroxyisoleucine analogs and their compositions for use in the prevention and treatment of obesity and related syndromes
INVENTOR(S): Chapal, Nicolas; McNicol, Patricia; Jette, Lucie
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 100 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006223884	A1	20061005	US 2006-387534	20060322
AU 2006256442	A1	20061214	AU 2006-256442	20060322
CA 2600954	A1	20061214	CA 2006-2600954	20060322
WO 2006131836	A2	20061214	WO 2006-IB2400	20060322
WO 2006131836	A3	20071004		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

EP 1874287	A2	20080109	EP 2006-779982	20060322

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU

WO 2007107008	A1	20070927	WO 2007-CA471	20070322

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

IN 2007DN07274	A	20071026	IN 2007-DN7274	20070920

PRIORITY APPLN. INFO.:	US 2005-664038P	P	20050322
	US 2006-387534	A	20060322
	US 2006-785174	A	20060322

WO 2006-IB2400 W 20060322
US 2006-836648P P 20060810
OTHER SOURCE(S): MARPAT 145:397785
AB The invention relates to 4-hydroxyisoleucine isomers and analogs R4-X-CR1aR1bCR2aR2bCR3(B)A [I; A = CO2H and derivs., C(O)SH and derivs., CONH2 and derivs., an acyl group, SO3H, etc.; B = amino group, including N-protected amino; X = O, S, NH or substituted imino; R1a, R1b, R2a, R2b, R3, R4 = H, (un)substituted alkyl, cycloalkyl, etc.; R1aCCR2a = (un)substitute mono or fused ring; R2a and R2b = CO, alkylimino, or alkylidene] and to their pharmaceutically acceptable lactones, salts, metabolites, solvates and/or prodrugs, to processes for their prepn., and to their pharmaceutical compns. useful for preventing and treating obesity and related syndromes. The invention also relates to a method of preventing the onset or progression of excessive wt. gain in a mammal (e.g., where the onset or progression of the wt. gain is assocd. with administration of one or more antidiabetic agents that stimulate wt. gain in the mammal) by administering to said mammal one of compds. I. Thus, reacting 5-tert-butylisoxazole-3-carboxylic acid with H2 in EtOH/H2O in the presence of Raney-Ni, and Pd/C gave 2-amino-4-hydroxy-5,5-dimethylhexanoic acid (II). (+)-(2S,3R,4S)-4-hydroxyisoleucine (III) in combination with rimonabant showed an enhanced effect on body wt. redn in the diet-induced obese C57BLU6 mice. II showed a greater efficacy on body wt. redn than III.

L9 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:395137 CAPLUS
DOCUMENT NUMBER: 142:423860
TITLE: Methods and compositions using hydroxylated amino acids and additional antidiabetic agents for use in the treatment of ***diabetes***
INVENTOR(S): Bellini, Francesco; Vezeau, Claude; Ribes, Gerard; Chapal, Nicolas; Prentki, Marc
PATENT ASSIGNEE(S): Innodia Inc., Can.
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005039626	A2	20050506	WO 2004-CA1883	20041027

WO 2005039626 A3 20050616
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2004282999 A1 20050506 AU 2004-282999 20041027
CA 2543498 A1 20050506 CA 2004-2543498 20041027
EP 1701735 A2 20060920 EP 2004-789790 20041027
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
BR 2004015781 A 20061226 BR 2004-15781 20041027
CN 1921881 A 20070228 CN 2004-80031719 20041027
JP 2008500955 T 20080117 JP 2006-537018 20041027
MX 2006PA04698 A 20060705 MX 2006-PA4698 20060426
IN 2006DN02881 A 20070803 IN 2006-DN2881 20060522
US 2007004623 A1 20070104 US 2006-577512 20060710
PRIORITY APPLN. INFO.: US 2003-514738P P 20031027
WO 2004-CA1883 W 20041027

AB The invention discloses methods and compns. for treating ***diabetes*** which involve the use of hydroxylated amino acids, e.g. 4-hydroxyisoleucine, and one or more addnl. antidiabetic agents.

L9 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:490279 CAPLUS
DOCUMENT NUMBER: 145:389086
TITLE: Hypoglycemic activity of the combination of active ingredients isolated from Trigonella foenumgraecum in alloxan induced ***diabetic*** mice
AUTHOR(S): Shah, Shweta Narendra; Bodhankar, Subhash Laxmanrao; Bhonde, Ramesh; Mohan, V.
CORPORATE SOURCE: Department of Pharmacology, Poona College of Pharmacy, Bharati Vidyapeeth Deemed University, Pune, 411038, India
SOURCE: Pharmacologyonline (2006), (1), 65-82
CODEN: PHARI3; ISSN: 1827-8620
URL: http://www.pharmacologyonline.unisa.it/archivies/

2006/5_Shah.pdf
PUBLISHER: University of Salerno
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB The aim of the study was to evaluate the hypoglycemic activity of two compds. isolated from seeds of Trigonella foenumgraecum viz; 4 hydroxyisoleucine and trigonelline in alloxan induced ***diabetic*** mice. The compds. were isolated by column chromatog. from fenugreek seeds. The combination of 4 hydroxyisoleucine and trigonelline [4HIT, 40:30, 120 mg/kg] was administered orally in alloxan induced ***diabetic*** mice. The parameters studied were blood glucose, histol. of pancreas, body wt., mortality and acute oral toxicity. 4HIT (120 mg/kg) showed redn. in blood glucose level within 2h and reduced the peak blood glucose level at 6h during acute study. After 28 days treatment with 4HIT, there was significant decrease in blood glucose level. 4HIT increased the glucose threshold as compared to only alloxan treated group. Histol. of pancreas showed formation of new islets near the vicinity of the pancreatic duct. Decreased glycosylated Hb adds to the effect of 4HIT. Glyburide was used as a std. antidiabetic drug and its effect on pancreatic cell was also studied. The pancreatic beta cells of glyburide treated mice did not show any islets in the vicinity of pancreatic duct. Both 4HIT and glyburide arrested the decrease in body wt. and mortality of ***diabetic*** mice. LD50 was found to be more than 5000 mg/kg. These results suggests that 4HIT showed hypoglycemic effect in alloxan induced ***diabetic*** mice. The presence of the pancreatic islets in the vicinity of duct suggested 4HIT might act by regeneration of new islets.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:740803 CAPLUS
DOCUMENT NUMBER: 145:195577
TITLE: Method for manufacturing traditional Chinese medicine composition extracted from Trigonella foenum-graecum seed and Morus alba for treating ***diabetes*** mellitus
INVENTOR(S): Yao, Chen; Lin, Yang; Zhang, Chao
PATENT ASSIGNEE(S): Chengdu Wagott Pharmaceutical Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 7pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1692922	A	20051109	CN 2005-10020691	20050411

PRIORITY APPLN. INFO.: CN 2005-10020691 20050411

AB The title traditional Chinese medicine is manufd. from (by wt. parts): Trigonella foenum-graecum seed 1-5 and Morus alba leaf 1-6. The title method comprises: (1) extg. Trigonella foenum-graecum seed with 50-95% ethanol under reflux, recovering ethanol to obtain concd. soln., sepg. with cation exchange resin, eluting with ammonia water, and concg. the eluate to obtain ext., (2) decocting Morus alba leaf in water, filtering, and drying the residue to obtain powder ext., and (3) mixing the above exts., adding adjuvants, and making into the final product. This traditional Chinese medicine compn. can be made into capsules, tablets, granules, pills, and soft capsules. This traditional Chinese medicine compn. has the advantages of good stability and good therapeutic effect, and can be used for lowering blood glucose and treating ***diabetes*** mellitus.

L9 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1994:280270 CAPLUS
DOCUMENT NUMBER: 120:280270
TITLE: Pharmaceutical compositions containing mono or polyhydroxylated amino acids for the treatment of non-insulin dependent ***diabetes*** mellitus
INVENTOR(S): Sauvaire, Yves; Ribes, Gerard
PATENT ASSIGNEE(S): Laboratoires Monal, Fr.
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 587476	A1	19940316	EP 1993-402135	19930901
EP 587476	B1	19980318		
R: AT, BE, CH, DE, DK, ES, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
FR 2695317	A1	19940311	FR 1992-10644	19920907
FR 2695317	B1	19950310		

JP 06157302	A	19940603	JP 1993-217588	19930901
AT 164064	T	19980415	AT 1993-402135	19930901
ES 2116421	T3	19980716	ES 1993-402135	19930901
CA 2105502	A1	19940308	CA 1993-2105502	19930903
CA 2105502	C	20001121		
IN 183194	A1	19991002	IN 1994-DE244	19940301

PRIORITY APPLN. INFO.: FR 1992-10644 A 19920907

AB The title amino acids are extd. from plants and are used as antidiabetic agents. Thus, 4-hydroxyisoleucine was extd. from fenugreek seeds (prepn. given) and used at 500.mu.M on isolated rat pancreas in presence of 8.3mM glucose for 10min. The amt. of insulin secreted was 2206 as compared to 810.mu.M.

L9 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:783081 CAPLUS
DOCUMENT NUMBER: 141:343238
TITLE: Insulinotropic agent ID-1101 (4-hydroxyisoleucine) activates insulin signaling in rat
AUTHOR(S): Broca, Christophe; Breil, Vincent; Cruciani-Guglielmacci, Celine; Manteghetti, Michele; Rouault, Christine; Derouet, Michel; Rizkalla, Salwa; Pau, Bernard; Petit, Pierre; Ribes, Gerard; Ktorza, Alain; Gross, Rene; Reach, Gerard; Taouis, Mohammed
CORPORATE SOURCE: Laboratoire de Pharmacologie, Centre de Pharmacologie et Biotechnologies pour la Sante-Unite Mixte de Recherche 5160, Faculte de Medecine, Centre National de la Recherche Scientifique, Montpellier, 34060, Fr.
SOURCE: American Journal of Physiology (2004), 287(3, Pt. 1), E463-E471
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB ID-1101 (4-hydroxyisoleucine), an amino acid extd. from fenugreek seeds, exhibits an interesting glucose-dependent insulin-stimulating activity. The present study was undertaken to investigate a possible extrapancreatic effect of ID-1101 on insulin signaling and action besides its previously described insulinotropic action. Insulin-sensitizing effects of ID-1101 were investigated in rat in vivo by three different approaches: (1) using euglycemic hyperinsulinemic clamps in two different rat models of insulin resistance, i.e., Zucker fa/fa rats and rats fed a sucrose-lipid diet; (2) measuring liver and muscle phosphatidylinositol (PI) 3-kinase activity after an acute injection of ID-1101 in normal and insulin-resistant

diabetic rats; and (3) after chronic treatment in two rat models of insulin resistance. Euglycemic hyperinsulinemic clamp expts. revealed that ID-1101 can improve insulin resistance through an increase of peripheral glucose utilization rate in sucrose-lipid-fed rats and by decreasing hepatic glucose prodn. in Zucker fa/fa rats. Moreover, we demonstrated that a single injection of ID-1101 activates the PI 3-kinase activity in liver and muscle from normal rats but also in muscle from ***diabetic*** rats. Finally, chronic ID-1101 treatment significantly reduced insulinemia in type 2 ***diabetic*** rats and reduced the progression of hyper-insulinemia in insulin-resistant obese Zucker fa/fa rats. These findings clearly demonstrate that ID-1101 can reduce insulin resistance through activation of the early steps of insulin signaling in peripheral tissues and in liver. In summary, ID-1101, besides its insulinotropic effect, directly improves insulin sensitivity, making it a potentially very valuable therapeutic agent for ***diabetes*** treatment.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:357928 CAPLUS
DOCUMENT NUMBER: 147:85854
TITLE: Advances in the study on 4-Hydroxyisoleucine
AUTHOR(S): Liu, Ling; Ding, Yongliang; Zhang, Guolin
CORPORATE SOURCE: Chengdu Institute of Biology, Chinese Academy of Sciences, Chengdu, 610041, Peop. Rep. China
SOURCE: Tianran Chanwu Yanjiu Yu Kaifa (2006), 18(3), 491-496
CODEN: TCYKE5; ISSN: 1001-6880
PUBLISHER: Tianran Chanwu Yanjiu Yu Kaifa Bianjibu
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review with 25 refs. on advances in the study on 4- Hydroxyisoleucine. 4-Hydroxyisoleucine is a new insulinotropic agent which can be used for the treatment of non-insulin-dependent ***diabetes*** mellitus. Progress of the study on existence, bioactivity, isolation and synthesis of 4-hydroxyisoleucine was reviewed.

L9 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:673816 CAPLUS
DOCUMENT NUMBER: 147:87676
TITLE: Hydantoins with insulinotropic action
INVENTOR(S): Ouazzani, Jamal; Sergent, Didier; Cortial, Sylvie; Sasaki, Nobumichi Andre; Potier, Pierre; Wang, Zhu

Qian
PATENT ASSIGNEE(S): Pharmamens, Fr.
SOURCE: Fr. Demande, 32pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2894962	A1	20070622	FR 2005-12934	20051220
WO 2007071728	A1	20070628	WO 2006-EP70006	20061220

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: FR 2005-12934 A 20051220
OTHER SOURCE(S): MARPAT 147:87676
GI

AB The invention discloses hydantoins I [R1, R2 = C1-6 alkyl, aryl, aralkyl; R3, R4 = H, C1-6 alkyl, aryl, aralkyl; or if R4 = H, tautomeric form II (R1-R3 as above) or tautomeric form III (R1-R3 as above)], or pharmaceutically acceptable addn. salts, isomers, enantiomers, diastereoisomers, or mixts thereof. The invention also discloses prepn. methods and use of these compds. in the treatment of the ***diabetes***
.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:170340 CAPLUS
DOCUMENT NUMBER: 144:239980
TITLE: Dietary supplement for suppressing appetite, enhancing and extending satiety, improving glycemic control, and stimulant free
INVENTOR(S): Needleman, Alvin; Needleman, Harriet
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 6 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006040003	A1	20060223	US 2004-786344	20040810

PRIORITY APPLN. INFO.: US 2004-786344 20040810

AB This invention relates to a nutritional intervention compn. for enhancing satiety prior to a meal and extending satiety after a meal. The nutritional intervention compn. decreases food intake producing wt. loss over time. The compn. consists of niacin, vitamin B6, calcium, phosphorous, magnesium, chromium, chitosan, fenugreek, ginseng, white willow bark, garcinia cambogia, aloe vera gel powder, momordica charantia, griffonia simplicifolia, lagerstroemia speciosa and vanadyl sulfate. The invention does not require stimulants or anabolic ingredients. There are three phases of activity within the compn. One, enhanced satiety through elevated serotonin. Two, improved carbohydrate metab., reduced blood glucose and slowed gastric emptying. Three, enhanced fiber binding of lipids and excess bile acids (no data).

L9 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1114726 CAPLUS
DOCUMENT NUMBER: 145:425782
TITLE: Antidiabetic composition comprising extracts of mulberry leaves containing 1-deoxynojirimycin and fenugreek seed containing 4-hydroxyisoleucine
INVENTOR(S): Seol, Seok Hwan; Yoon, Won Joo; Park, Hyung Hwan; Kwon, Ik Boo
PATENT ASSIGNEE(S): Lotte Confectionery Co., Ltd., S. Korea
SOURCE: Repub. Korean Kongkae Taeho Kongbo, No pp. given

CODEN: KRXXA7
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 2006033837	A	20060420	KR 2004-82926	20041016

PRIORITY APPLN. INFO.: KR 2004-82926 20041016

AB An anti- ***diabetic*** compn. comprising ext. of mulberry leaves and ext. of fenugreek seed is provided to show higher blood sugar-decreasing effect than that comprising either the ext. of mulberry leaves or the ext. of fenugreek seed. The anti- ***diabetic*** compn. comprises 25-75% of mulberry leaf ext. contg. at least 0.4% of 1-deoxynojirimycin, and 25-75% of fenugreek seed ext. contg. at least 5% of 4-hydroxyisoleucine. The compn. further comprises 10-50% of at least one selected from the group consisting of evening primrose oil, silk protein, ginko ext. and mixts. thereof.

L9 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:617969 CAPLUS
DOCUMENT NUMBER: 127:257635
TITLE: Antidiabetic composition containing (2S, 3R, 4S)-4-hydroxyisoleucine
INVENTOR(S): Sauvaire, Yves; Ribes, Gerard
PATENT ASSIGNEE(S): Societe Civile de Gestion Jouvenet, Fr.; Sauvaire, Yves; Ribes, Gerard
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9732577	A1	19970912	WO 1997-FR420	19970307

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

FR 2745718	A1	19970912	FR 1996-2955	19960308
FR 2745718	B1	19980507		
AU 9720319	A	19970922	AU 1997-20319	19970307

PRIORITY APPLN. INFO.: FR 1996-2955 A 19960308
WO 1997-FR420 W 19970307

AB An antidiabetic compn. capable of stimulating insulin secretion and particularly suitable for treating non-insulin-dependent ***diabetes*** is disclosed. The compn. contains (2S, 3R, 4S)-4-hydroxyisoleucine, and/or the lactone form thereof, and is substantially free of any other stereoisomer of this compd.

L9 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1251600 CAPLUS
DOCUMENT NUMBER: 144:45300
TITLE: 4-Hydroxyisoleucine an unusual amino acid as antidyslipidemic and antihyperglycemic agent
AUTHOR(S): Narender, Tadigoppula; Puri, Anju; Shweta; Khaliq, Tanvir; Saxena, Rashmi; Bhatia, Geetika; Chandra, Ramesh
CORPORATE SOURCE: Division of Medicinal and Process Chemistry, Central Drug Research Institute, Lucknow, India
SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(2), 293-296
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Trigonella foenum-graecum, commonly known as fenugreek, is an annual herbaceous plant. From the seeds of T. foenum-graecum an unusual amino acid, 4-hydroxyisoleucine, has been isolated, which significantly decreased the plasma triglyceride levels by 33% ($P < 0.002$), total cholesterol (TC) by 22% ($P < 0.02$), and free fatty acids by 14%, accompanied by an increase in HDL-C/TC ratio by 39% in the dyslipidemic hamster model.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:167800 CAPLUS
DOCUMENT NUMBER: 134:202704

TITLE: Use of amino acids for making medicines for treating insulin-resistance

INVENTOR(S): Ribes, Gerard; Taouis, Mohammed; Petit, Pierre Roger; Broca, Christophe; Sauvaire, Yves; Pau, Bernard

PATENT ASSIGNEE(S): Centre National de la Recherche Scientifique (CNRS), Fr.; Institut National de la Recherche Agronomique (INRA)

SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001015689	A1	20010308	WO 2000-FR2361	20000823
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2797767	A1	20010302	FR 1999-10874	19990827
FR 2797767	B1	20020614		
CA 2382835	A1	20010308	CA 2000-2382835	20000823
EP 1206257	A1	20020522	EP 2000-958726	20000823
EP 1206257	B1	20041103		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003508435	T	20030304	JP 2001-519903	20000823
EP 1421937	A1	20040526	EP 2003-291523	20000823
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
AT 281159	T	20041115	AT 2000-958726	20000823
PT 1206257	T	20050331	PT 2000-958726	20000823
ES 2231247	T3	20050516	ES 2000-958726	20000823
ZA 2002001619	A	20030526	ZA 2002-1619	20020226
HK 1052456	A1	20051028	HK 2002-108489	20021122

PRIORITY APPLN. INFO.: FR 1999-10874 A 19990827

EP 2000-958726 A3 20000823
WO 2000-FR2361 W 20000823

AB The invention concerns the use of monohydroxy or polyhydroxy amino acids, and the lactone forms thereof for making medicines with insulin-analog and/or insulin-sensitizing effects on peripheral tissues targeted by insulin, and more particularly the use thereof for making medicines for treating and preventing insulin-resistance. Injection of 200 .mu.g/kg 4-hydroxy isoleucine i.p. induced the activation of insulin receptor and insulin receptor substrate-1 which was comparable to insulin injection.

L9 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:70710 CAPLUS
DOCUMENT NUMBER: 128:200858
TITLE: 4-Hydroxyisoleucine: a novel amino acid potentiator of insulin secretion
AUTHOR(S): Sauvaire, Yves; Petit, Pierre; Broca, Christophe; Manteghetti, Michele; Baissac, Yves; Fernandez-Alvarez, Josepha; Gross, Rene; Roye, Michele; Leconte, Agnes; Gomis, Ramon; Ribes, Gerard
CORPORATE SOURCE: Laboratoire de Recherche sur les Substances Naturelles Vegetales, Unite Propre de Recherche Enseignement Superieur EA 1677, Universite Montpellier II, Montpellier, 34095, Fr.
SOURCE: Diabetes (1998), 47(2), 206-210
CODEN: DIAEAZ; ISSN: 0012-1797
PUBLISHER: American Diabetes Association
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors report the characterization of a new insulinotropic compd., 4-hydroxyisoleucine. This amino acid has been extd. and purified from fenugreek seeds, which are known in traditional medicine for their antidiabetic properties. 4-Hydroxyisoleucine increases glucose-induced insulin release, in the concn. range of 100 .mu.M to 1 mM, through a direct effect on isolated islets of Langerhans from both rats and humans. The stimulating effect of 4-hydroxyisoleucine was strictly glucose dependent; indeed, ineffective at low (3 mM) or basal (5 mM) glucose concns., the amino acid potentiated the insulin secretion induced by supranormal (6.6-16.7 mM) concns. of glucose. In addn., in the isolated perfused rat pancreas, the authors could show (1) that the pattern of insulin secretion induced by 4-hydroxyisoleucine was biphasic, (2) that this effect occurred in the absence of any change in pancreatic .alpha.- and .delta.-cell activity, and (3) that the more glucose concn. was increased, the more insulin response was amplified. Moreover,

4-hydroxyisoleucine did not interact with other agonists of insulin secretion (leucine, arginine, tolbutamide, glyceraldehyde). Therefore, the authors conclude that 4-hydroxyisoleucine insulinotropic activity might, at least in part, account for fenugreek seeds' antidiabetic properties. This secretagogue may be considered as a novel drug with potential interest for the treatment of NIDDM.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:714049 CAPLUS
DOCUMENT NUMBER: 132:44784
TITLE: 4-Hydroxyisoleucine: experimental evidence of its insulinotropic and antidiabetic properties
AUTHOR(S): Broca, Christophe; Gross, Rene; Petit, Pierre; Sauvaire, Yves; Manteghetti, Michele; Tournier, Michel; Masiello, Pellegrino; Gomis, Ramon; Ribes, Gerard
CORPORATE SOURCE: Unite Mixte de Recherche 9921 du Centre National de la Recherche Scientifique, and Faculte de Medecine and Laboratoire de Recherche sur les Substances Naturelles Vegetales, UPRES EA 1677, Laboratoire de Pharmacologie, Montpellier, 34060, Fr.
SOURCE: American Journal of Physiology (1999), 277(4, Pt. 1), E617-E623
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have recently shown in vitro that 4-hydroxyisoleucine (4-OH-Ile), an amino acid extd. from fenugreek seeds, potentiates insulin secretion in a glucose-dependent manner. The present study was designed to investigate whether 4-OH-Ile could exert in vivo insulinotropic and antidiabetic properties. For this purpose, i.v. or oral glucose tolerance tests (IVGTTs and OGTTs, resp.) were performed not only in normal animals but also in a type II ***diabetes*** rat model. During IVGTT in normal rats or OGTT in normal dogs, 4-OH-Ile (18 mg/kg) improved glucose tolerance. The lactonic form of 4-OH-Ile was ineffective in normal rats. In non-insulin-dependent ***diabetic*** (NIDD) rats, a single i.v. administration of 4-OH-Ile (50 mg/kg) partially restored glucose-induced insulin response without affecting glucose tolerance; a 6-day subchronic administration of 4-OH-Ile (50 mg/kg, daily) reduced basal hyperglycemia, decreased basal insulinemia, and slightly, but significantly, improved

glucose tolerance. In vitro, 4-OH-Ile (200 .mu.M) potentiated glucose (16.7 mM)-induced insulin release from NIDD rat-isolated islets. So, the antidiabetic effects of 4-OH-Ile on NIDD rats result, at least in part, from a direct pancreatic B cell stimulation.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1066377 CAPLUS
DOCUMENT NUMBER: 145:396574
TITLE: A method and composition for nutritionally improving glucose control and insulin action
INVENTOR(S): Hayes, Kenneth C.; Greenberg, Norman Alan; Troup, John P.; Falk, Anne L.; Biolo, Gianni
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE: PCT Int. Appl., 145pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006108008	A2	20061012	WO 2006-US12576	20060404
WO 2006108008	A3	20070118		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

AU 2006231557	A1	20061012	AU 2006-231557	20060404
CA 2601427	A1	20061012	CA 2006-2601427	20060404
EP 1868454	A2	20071226	EP 2006-749290	20060404

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR

IN 2007DN07230 A 20071012 IN 2007-DN7230 20070919
PRIORITY APPLN. INFO.: US 2005-668633P P 20050406
WO 2006-US12576 W 20060404

AB Disclosed is a method and compn. for nutritionally improving glucose and insulin balance in an individual. The invention further provides a method for treating a comorbidity of ***diabetes*** . In one embodiment, the invention provides a nutritional formulation comprising: a protein source, a fat source, and a carbohydrate source, wherein the protein source, the fat source, and the carbohydrate source are in a ratio of about 1:1:1, each comprising about one third of the total calories of the compn.

L9 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:735361 CAPLUS
DOCUMENT NUMBER: 141:423478
TITLE: Genotoxicity testing of a fenugreek extract
AUTHOR(S): Flammang, A. M.; Cifone, M. A.; Erexson, G. L.; Stankowski, L. F.
CORPORATE SOURCE: Ross Products Division, Abbott Laboratories, Columbus, OH, 43215-1724, USA
SOURCE: Food and Chemical Toxicology (2004), 42(11), 1769-1775
CODEN: FCTOD7; ISSN: 0278-6915
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB As part of a safety evaluation of novel ingredients for use in blood glucose control, the potential genotoxicity of a fenugreek seed ext. (THL), contg. a min. of 40% 4-hydroxyisoleucine (4-OH-Ile), was evaluated using the std. battery of tests (reverse mutation assay; mouse lymphoma forward mutation assay; mouse micronucleus assay) recommended by US Food and Drug Administration (FDA) for food ingredients. THL was detd. not to be genotoxic under the conditions of the tested genetic toxicity battery. The neg. assay results provide support that addn. of THL to foodstuffs formulated for people with ***diabetes*** is expected to be safe. A wide safety margin is established, as anticipated doses are small compared to the doses administered in the assays.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT